

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: McTigue et al.

Serial No. NOT YET ASSIGNED

Filed: August 28, 3001

For: Modifications of VEGF Receptor-2 Protein  
and Method of Use

Art Unit: NOT YET ASSIGNED

Examiner: NOT YET ASSIGNED

Atty. Docket: 0125-0016D3

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Prior to examination of the above-identified application, Applicant herewith  
respectfully requests the following amendments:

IN THE CLAIMS:

Kindly delete claims 1-16 and replace with the following claims 17-26.

17. A method for screening compounds for RTK agonists or RTK antagonists comprising:
- (a) crystallizing a modified RTK polypeptide, said modified RTK polypeptide having kinase activity and comprising RTK kinase domain  $\alpha$  helix D linked to RTK kinase domain  $\alpha$  helix E by a truncated RTK kinase insert domain (KID);
  - (b) obtaining crystallography coordinates for said modified RTK polypeptide;
  - (c) applying said crystallography coordinates for said modified RTK polypeptide in order to generate a model of said RTK polypeptide suitable for use in designing molecules that will act as agonists or antagonists to said polypeptide; and

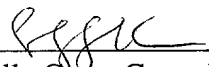
- (d) applying an iterative process whereby various molecular structures are applied to said model to identify agonists or antagonists to said modified RTK polypeptide.
18. The method of claim 17 wherein said truncated kinase insert domain comprises a deletion of 50 residues from the KID.
  19. The method of claim 17 wherein said truncated kinase insert domain comprises a deletion of 60 residues from the KID.
  20. The method of claim 17 wherein said truncated kinase insert domain comprises a deletion of the highly charged residues from the KID.
  21. The method of claim 17 wherein said truncated kinase domain linking said  $\alpha$  helix D to said  $\alpha$  helix E is of a sufficient length so as to allow said helices to maintain appropriate conformation associated with competent kinase structure.
  22. The method of claim 17 wherein said RTK polypeptide is a member of the PDGFR family.
  23. The method of claim 22 wherein said PDGFR member is selected from the group consisting of VEGFR-1, VEGFR-2, PDGFR- $\alpha$ , PDGFR- $\beta$ , stem cell growth factor receptor (c-kit), and colony stimulating factor-1 receptor (CSF-1R/c-fms).
  24. The method of claim 22 wherein said RTK polypeptide is selected from the group consisting of insulin receptor (IRK), fibroblast growth factor receptor-1 (FGFR-1), and VEGFR-2.
  25. The method of claim 17 wherein said RTK polypeptide is VEGFR-2.
  26. The method of claim 17 wherein said modified RTK polypeptide comprises VEGFR2 $\Delta$ 50 polypeptide of SEQ ID NO: 5.

REMARKS

It is respectfully requested that the Examiner enter these amendments prior to examining the application on its merits.

Respectfully submitted,

SHANKS & HERBERT

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